Papers and Originals

Some Reactions of the Nervous System to Trauma*

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I should like first to thank most warmly the staff of the famous Birmingham Accident Service for granting me the privilege of giving this important lecture. I am a great admirer of hospital accident services, and we will all agree, as Ruscoe Clarke demonstrated by his devoted example, that to provide a service is not enough: for it is necessary and expected of the leading exponents that they will also teach others and will pioneer new developments and organize research. Trauma to the nervous system provides many opportunities for research, and in the course of this talk I hope to refer to some of these.

Students of the nervous system and its diseases are dull indeed if they fail to use their great clinical opportunities to advance knowledge, and the effects of injury are particularly valuable for this purpose. Research on the nervous system, whether concerned with the brain or the peripheral nerve, is a leading challenge to man in the second half of this twentieth century. This is, I think, more appreciated in some other countries than here, and during the past 10 years, for example, research on the nervous system in the U.S.A. has come to be supported most lavishly by national funds.

In this country there seems to be something wrong with our research allocations, for the funds of the University Grants Committee, which are supposed to support research related to clinical specialties, rarely reach beyond the insatiable needs of the professorial units. In the U.S.A., on the other hand, the clinical specialties such as orthopaedics and neurology seem now almost to get preferential treatment, and this has led to an unfortunate situation in that our colleagues in the U.S.A. get all they can need, while we here struggle to get the simplest assistance from charity. The contrast is too extreme to be healthy, and some means of correcting what has become an intolerable situation is urgently called for.

First I should give a personal word of explanation, for, although a student of the effects of trauma to the nervous system for 35 years, I have rarely been intimately concerned with the present-day problems of the accident surgeon. Beginning in 1930 (Russell, 1932) with a study of 200 acute cases of closed head injury, there followed investigations of the traumatic amnesias, experimental concussion, the nerve injuries of war, wounds of the spinal cord and brain. A study of the effects of focal brain injury from a collection of 1,000 penetrating wounds of the brain is still being continued. Such a varied experience provides an outlook on trauma to the nervous system which is inevitably rather different from that of the accident surgeon, and yet I hope that some of my rather disjointed remarks on the subject will be of general interest.

The unique and peculiar properties of the nervous-system cells and tissue lead to many special considerations concerning the effects produced by trauma. From our point of view it seems best to consider that the chief concern of the nervous system is to provide a complex mechanism for communication between cell and cell or between cell and tissue. This forms a collection of computer-like arrangements which depend on the integrity and survival of the individual elements of the system, the nerve cells and their processes. The nerve-cell processes provide the means required for connexions between different parts of the central nervous system, and they form the white matter of the brain, the tracts in the spinal cord, and the conducting elements in the peripheral nerves. The relationship of these axons to their parent cell is a most remarkable one, and the fibre may be tens of thousands of times longer than the diameter of the cell body. Cut axons always attempt to grow again from the proximal end, but this is only functionally useful in the cases of peripheral nerves.

In some respects there are important similarities between the responses to injury of the brain, the spinal cord, and the peripheral nerves, and of course the peripheral nervous system is the easiest to study. Indeed, the study of nerve injuries provides important evidence regarding the general response of the nervous system to trauma, ischaemia, toxins, etc.

Injuries to Peripheral Nerves

The importance of peripheral nerves in relation to bodily growth is well known, and it is worth noting that the limb regeneration that occurs in newts and salamanders after amputation is dependent on the amputation stump being fully innervated (Kamkin and Singer, 1959). In man, the trophic effects of denervation are less dramatic but are still striking, and may, I suppose, play a part in the failure of limb development in the embryo in the thalidomide catastrophe. In studying nerve injuries we naturally note particularly the interference with conduction, and the combined study of the motor, sensory, and reflex disturbance enables the clinician in most instances to localize with precision the level at which a nerve or plexus is injured. The wounds of both world wars provided a vast variety of every type of nerve-injury study (often by direct section of the nerve involved), and, so far as the second world war is concerned, the records published of the British (Seddon, 1954) and American (*Surgery in World War II, U.S. Army,* 1959) experiences are noteworthy contributions which the respective medical services should be proud of. The traumatic neuropathies of civilian practice are in some respects more complex as regards aetiology, even though the choice of syndromes is relatively limited.

Like the central nervous system, the peripheral nerves are vulnerable to direct blows and distortions, and this often leads to an instantaneous loss of conduction. Sudden stretching of a peripheral nerve is particularly damaging and may be the mechanism underlying the sudden palsies that occasionally appear in relation to violent voluntary limb movement. For example, the radial nerve is sometimes put out of action in this way, either in the arm, through violent contraction of the

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triceps muscle, or in the forearm, where the dorsal interosseous nerve may be injured in relation to vigorous hand and wrist activity.

Median-nerve injury in the "carpal tunnel syndrome" is a good example of the combined effects of repeated stretching and pressing on a nerve.

The paralytic shoulder-girdle neuritis syndrome may have a somewhat similar mechanism, for the nerves and roots affected are those which are normally most subjected to stretch, and it seems probable to me that the pathology causing the intense shoulder-pain which precedes the palsy in this interesting syndrome also renders the nerves vulnerable to the stretches incurred by a normal range of activity, so that the palsy is actually often self-inflicted. Nevertheless, the mechanism of occupational traumatic neuropathies is sometimes obscure, as in a carpenter seen recently who within a space of a few weeks developed an almost complete lesion of the anterior interosseous branch of the median nerve in both forearms.

Pressure on nerves as a cause of paralysis or pain is a popular explanation of many traumatic nerve palsies, but often the situation is more complex than this, and many researches have been carried out in an endeavour to elucidate the factors involved. Severe compressions are of course so violent as to be disruptive and to behave like nerve section, but what are we to think of the intervertebral disk lesion with severe root pain?

Sudden distortion of a root causes a neuralgic pain, but prolonged pressure on a nerve usually blocks conduction by an ischaemic effect without causing pain. Observation by Cloward (1960) and others on the effect of stimulating an intervertebral disk at operation under local anaesthesia indicates a remarkable root-distribution of referred pain from the disks, the clinical features of which might easily be thought by the clinician to indicate nerve root compression.

Again, the sciatica which follows disk protrusion is often delayed for days after the protrusion occurs, and is associated with pain on root-stretching and perhaps tenderness down the course of the sciatic nerve. Some of these changes are obviously occurring in the interstitial tissues of the nerve over a substantial distance. These are certainly a consequence of a disk protrusion, but the term compression by the disk is not an explanation that fully accounts for the clinical features.

The experimental effects of nerve compression have been much studied by, for example, the elegant technique in trained volunteers of investigating the phenomena of "compression tingling" and "release pricking" during and after compression by a sphygmomanometer cuff (Merrington and Nathan, 1949). Peripheral nerves survive obstruction of the blood supply for very much longer than does the brain. Most of the experimental observations depend primarily on such an ischaemic lesion, and the common pressure palsies usually fall into this category. While many compressive nerve-blocks ("pressure palsies") recover within a few days or weeks, those that are most severe are obliged to recover by regeneration, with all the disadvantages and limitations inherent in the random axonal branching that occurs during regeneration. It is of interest to note that Bell's palsy, and also the delayed facial paralysis after fracture of the base of the skull, both behave like pressure palsies, and a proportion require to regenerate. It is most gratifying and exciting to hear, as I did recently in the U.S.A., such encouraging reports of the new techniques being used to graft nerve injuries with tubes of Milipore filter. If I may make a suggestion to accident surgeons, I think there is a need in this country at the present time for research units on nerve injuries, for many of the still unanswered questions are amenable to investigation by modern electro-physiological techniques. There also seems to be undue delay *before* the discoveries of the research zoologist or physiologist become applied to current medical and surgical practices in this field. Even the best way of treating denervated muscle is still uncertain. Thus, so far as one can judge, the old idea of keeping denervated muscle in a shortened state is basically wrong, but there are several doubts still to be clarified in relation both to this and to the problems of surgical repair.

Spinal Cord

The response of the spinal cord to injury is only too well known to you all. Here the effect of severe distorting forces is catastrophic and interruption of conduction is often complete and irrecoverable. All will agree that it is important in the early hours and days after traumatic paraplegia to search for the slightest evidence of some conduction past the site of injury, especially in cervical-cord lesions, where the proportion of incomplete lesions is higher than at other levels. Incomplete lesions demand every attention and device to reduce the hazard of further injury to the cord, and also to provide reasonable reduction of vertebral displacement so that partial recovery will not be upset years later by a local progressive myelopathy in relation to traumatic ridges and deformities of the spinal canal. When one is certain that the lesion is complete, then apart from avoiding serious spinal deformities active rehabilitation may presumably be encouraged with vigour from an early stage.

It is interesting to note that severed spinal-cord neurones have been shown to regenerate quite vigorously, especially under the influence of the so-called nerve growth factor (see Scott and Liu, 1963). Trevor Hughes and Brownell (1963) here in Oxford have on several occasions demonstrated regeneration of fibres in human spinal cord, but, alas, there is nothing to suggest that these new fibres are of any value to the patient's progress, though there are possibilities still of some advance in this field of research.

The part played by vascular damage and infarction in cases of traumatic myelitis is often uncertain, but may be clear if the disability presents with the well-known clinical features of, say, an anterior-spinal-artery thrombosis. It is noteworthy that the tragic cases of spinal artery thrombosis which affect young adults often report some minor spinal injury or strain a few hours before the disaster occurred: something perhaps which, owing to a local anatomical peculiarity, traumatizes an artery contributing to the spinal-cord supply. The vulnerability of the spinal cord in the elderly with cervical spondylosis is now well known, and the cord lesion in these cases is sometimes vascular and secondary to a traumatic thrombosis of one vertebral artery spreading to the upper part of the anterior spinal artery.

Experimental observations (see Tönnis, 1963) concerned with compression of the spinal cord indicate that the spinal cord after being rendered ischaemic will continue to conduct for 15 to 20 minutes before a flaccid paraplegia develops fully—this would suggest that, in the vascular type of acute myelitis, infarction occurs several minutes before the clinical features of paresis become very evident. The same of course applies to ischaemic lesions of peripheral nerves, especially those caused by thrombosis of the vasa nervorum, for in such instances conduction is likely to continue perhaps for hours after a vascular lesion.

It may here be repeated that spinal or nerve injuries which cause instantaneous paralysis, as with head injuries which cause instantaneous loss of consciousness, cannot possibly depend on the kind of compression which merely blocks blood supply, for ischaemic lesions are always much more gradual in their effects on the nervous system.

Reorganization of Spinal-cord Activity

Although spinal-cord neurones never regenerate usefully across the gap caused by transection, there is, in partial lesions, a very remarkable clinical progress, and it is for this reason that the faintest evidence of cord conduction after trauma is most encouraging and important. If there is then even a trace of

voluntary movement from muscles below the lesion, or any appreciation of a very vigorous and even traumatic sensory stimulus within a few hours of the injury, then a satisfactory recovery may often occur.

The strength of voluntary movements seems to increase steadily in these cases for nine to twelve months, as indeed happens in paralytic poliomyelitis. This long period cannot possibly depend simply on the resolution of oedema or of inflammatory reaction. It seems increasingly likely that during this period the active use of surviving neurones leads to a plastic reorganization of neuronal communication, so that surviving units come to control neurones below the level more effectively. A determined voluntary attempt to move is the most useful physiological stimulus in this situation, but of course contractures at hip and knee must always be prevented. This reorganization presumably involves micro-alterations in the structure of synapses comparable to those which must occur in response to learning a motor skill.

Commotio Cerebri

The effects of trauma on differing parts of the nervous system have therefore both similarities and differences. All parts are vulnerable to stretching, to direct disruptive forces, and to ischaemia, but on the other hand there are also striking differences. A peripheral nerve or a nerve tract consists of a collection of axons, and these will survive ischaemia for very much longer than will the neuronal-cell body itself. Thus in lesions of cervical enlargement of the cord, whether ischaemic or traumatic, there may be severe permanent atrophic paralysis of upper-limb muscles, while the control of the lower limbs is little affected. The ischaemia being limited, and though fatal to the motor cells, is relatively harmless to the tracts.

Brain cells are also extremely vulnerable to anoxia, and this is certainly a cause of death in some cases of head injury which have experienced an episode of respiratory or circulatory collapse.

During and after the second world war we collected in Oxford the brains of some patients who survived for weeks or months with profound traumatic dementia and rigidity of the limbs. Some of these brains appeared to be remarkably normal on naked-eye examination, and the question naturally arose whether an episode of anoxia had caused these disastrous effects.

Dr. Strich (1956), under the direction of Dr. Peter Daniel, investigated this problem and found little or no evidence of anoxic cortical-cell loss. On the other hand, she found profound degenerative changes throughout the white matter of the cerebral hemisphere which indicated a primary destruction of the tracts in the central white matter. This observation was of great importance, for it indicated that distorting forces within the brain had destroyed tracts without producing any visible naked-eye lesion. This was especially significant, for these forces had been worked out theoretically by a physicist years previously (Holbourn, 1943), while the forceful movement of parts of the brain one on another had been photographed by Pudenz and Shelden (1946). The clinical features also indicated that in concussion a direct injury to neurones must be the basic mechanism (Russell, 1932).

All these observations support each other so clearly that it is reasonable now to look on the gross lesions described by Strich as being similar in mechanism to those which cause minor concussion, except of course that they are much less severe in the latter—the recoverable injuries.

Present-day research apparatus makes it possible to answer the old questions of what goes on in the brain during concussion. Accelerometers, high-speed pressure recorders, and concussion-guns are the magic instruments for this purpose, and some important studies are appearing, such as those by Unterharnscheidt (1963), Sellier and Unterharnscheidt (1963), and Ommaya (1963). Careful analysis and recording of respiratory and biochemical abnormalities obviously give much valuable information, as is seen in recent studies by Huang *et al.* (1963) and by Frowein (1963).

The importance of acceleration in relation to head injury has been fully supported by these studies, and it seems that the human brain may survive accelerations of 400–600 *g* for a few milliseconds. The contrecoup lesions are evidently due to a destructive negative-pressure effect, as has been illustrated in recent years by many writers on the subject.

During the present century there have been sporadic fashions in attributing the effects of head injury to such influences as transient cerebral anaemia (Trotter, 1924), capillary haemorrhages in the brain stem (Duret (1878) lesions) and cerebral oedema. In the 1930s the obsession with cerebral oedema was so strong that in many centres extremely active measures were adopted, such as repeated lumbar puncture, forbidding fluids, and nursing in a sitting-up position. These ideas are now thought to be generally mistaken, but occasionally any one of them may assume importance and significance. The mistake was to try to explain basic neuronal trauma in terms of vascular complications which are, in fact, only rarely of much importance.

One surprising feature of injury to the nervous system is that there is a remarkable relationship between the severity of the injury and the duration of disturbed function. This is particularly well seen in cerebral commotion, for the duration of disturbed consciousness seems in most instances to bear a fairly close relation to the severity of brain damage.

As regards treatment, I doubt whether we can expect many improvements so far as the best centres are concerned, for already some completely hopeless cases are being kept alive, and nobody hopes for more success in that direction. Recent important advances include the full recognition by first-aid teachers of the need for postural drainage to protect the lungs and the usefulness of tracheostomy after admission for the worst cases. However, although standards in a few centres have become so very good, there is a vast need for the expert knowledge regarding all types of trauma to be made available to a much wider public than is possible at present.

Those who study the post-mortem findings in fatal injuries may get an entirely misleading impression regarding the significance of the vascular complications, for it is often extremely difficult at necropsy to determine the precise cause of death. The presence of a very visible abnormality such as a subdural or extradural haemorrhage, an area of cortical contusion, or a small brain-stem haemorrhage, frequently leads to unjustified conclusions, for these visible lesions seen at necropsy can only be assessed, and then only approximately, by detailed consideration of the clinical features, as well as the post-mortem findings. Unfortunately the disruptive lesions described by Dr. Strich are not easy to demonstrate when death occurs within a day or two of the injury, so that the most important lesion of all remains undetected as regards severity.

Under these circumstances the significance of, say, an extradural haemorrhage may be extremely difficult to assess, so that statistics from different centres are usually impossible to compare. Exploratory craniotomy in a hopeless case of head injury will often reveal some extradural or subdural haemorrhage, but it is absurd to include such a fatality in the statistics of the surgery of extradural haemorrhage. Similarly, where all severe head injuries are subjected to exploratory craniotomy the statistics must be very good if small collections of extradural blood are included as instances of extradural clot.

I am not hopeful, therefore, about there being any great advances in the treatment of head injury, and we can only hope that people will come to realize that the possibilities of severe head injury should be reduced each year and not

increased as at present. We who see again and again the tragedies caused by head injury become highly critical and resentful of this waste of human brain. We all have our own cures for this disgraceful state of affairs, but most of us find it useless to express our personal views. I am delighted, therefore, to note that the Accident Services are coming to play an important part in educating the public and our legislators in this matter.

While I cannot feel hopeful that we can learn many better ways to treat the acute stage of head injury, we can always improve the rehabilitation services. During the war there were many good rehabilitation arrangements, and it is unfortunate that the service for civilians in this field is now relatively inferior.

Although research on head injuries may do little to save those cases which crowd our accident wards, there is still a great opportunity to study the effects on brain function and thus to increase our knowledge of cerebral mechanisms. For this purpose I would specially advise a close link with the experimental psychologists, since this group of scientists are at the present time making many important contributions to knowledge of how the brain works ; and these researches are not only of academic interest ; they also lead to improved techniques for the assessment of defective function of that greatest problem and challenge of nature, the human brain.

Research on Remembering

It is worth noting that much present-day conception of memory processes is profoundly influenced by the main characteristics of the traumatic amnesias.

Thus there is conclusive evidence now that in order to remember an event for future use the brain must subsequently have a certain uninterrupted period of normality for the event to be held. The phenomenon of retrograde amnesia (R.A.) in relation to concussion played an important part in the elucidation of this conception, and the same R.A. is observed in relation to an electrically induced convulsion (E.C.T.). Experimental confirmation of this time factor has been provided by giving E.C.T. to rats at different intervals after a training-run to learn a simple maze (Gerard, 1961): it is found that E.C.T. a few minutes or even half an hour after the training-run interferes with learning, while if given at an interval of 2–3 hours after the run it has no harmful effect. It looks as though our memories may be dependent on a dynamic process and not a static arrangement. This dynamic process must maintain fine alterations in synaptic mechanisms, perhaps by the spontaneous activity of neurones, which is sufficiently stable to withstand the effects of anaesthesia or hypothermia. Occasionally during or shortly after the acute effects of a head injury the patient has some visual phenomenon or hallucination of an event just preceding the injury which is never properly remembered as the event falls within the R.A. These half-memories (see Russell, 1959) may be informative to the intelligent recorder of the case, and may perhaps sometimes, for the patient, lead through confabulation to a series of grotesquely false accusations on how the injury occurred.

Another observation of fundamental importance to the study of memory is that recent memories are relatively vulnerable to the effects of concussion. This is seen in students after such an injury, for their memory of recent studies and even of recently acquired skills is often found to be relatively defective. Further, during the stages of recovery the R.A. may at first extend over several years, and the remarkable " shrinkage " of the R.A. is a frequently observed and very important phenomenon.

During the period of traumatic confusion, even at times when behaviour appears to be normal, current events are not stored, so that there is a complete absence of memorizing—" amnésie de mémoration " (Barbizet, 1963)—and as the duration of this state usually bears a fair relationship to the seriousness of an uncomplicated closed head injury the duration of post-traumatic amnesia is an important feature of any case.

When we come to a study of the physiology of behaviour and personality, then the effects of severe head injury assume special interest in relation to the patient's age.

The young adult whose brain is trained, or if you prefer is running in well-established grooves, can adapt to very severe injury with surprising success, although his personal traits may become accentuated ; but in young children the position is much more disturbing, for the laborious process of training is only begun and any physical defect in " the computers " makes education a hundred times harder. As with encephalitis, therefore, severe head injury may render a young child virtually unresponsive to education—a major tragedy.

With the old, on the other hand, the senile changes are already leading to a mild dementia, and a severe head injury makes the brain perhaps 10 years older, with a tremendous loss of capacity, memories old and new, and changes in personality. It is often said of the old " he was never himself again after his fall."

I have mentioned these few aspects of brain mechanism, for I feel sure that an interest in these remarkable phenomena will enliven the work of any accident service ; and they are of course phenomena which in general can be studied only in man.

There is much more still to be learned from a clinical bedside study of commotio cerebri, and I would commend the subject as one of exceptional interest and considerable importance.

Summary

Injury to peripheral nerve, spinal cord, and brain may be compared in different ways, and several striking resemblances and differences appear.

In all instances there is an interruption of conduction, and when the axons are severed they attempt to regenerate : this sprouting, however, is useful only in the case of peripheral nerve injuries.

The trophic influences of peripheral nerves are essential for the limb regeneration that occurs in newts, and an embryonic neuropathy may be responsible for the thalidomide catastrophes.

Recovery from partial spinal-cord injuries may be related to a reorganization of the connexions of surviving neurones.

In the case of closed head injuries, acceleration forces are important, and the human head (and brain) may survive 500 *g* for a few milliseconds. The demonstration of widespread axonal severing confirms the importance of direct fibre-destruction without there being necessarily much vascular damage.

The clinical features of cerebral commotion provide many valuable opportunities for the study of brain mechanisms.

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Daily Haemodialysis in "Hypercatabolic" Acute Renal Failure

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The value of early and frequent haemodialysis in the management of acute "hypercatabolic" renal failure (daily plasma-urea increment exceeding 60 mg./100 ml.) is well established (Parsons *et al.*, 1961).

The problem of increasing the number of haemodialyses for the individual patient with acute renal failure has been solved regarding the requirement for repeated access to the vascular bed by the use of a silastic-teflon arteriovenous shunt (Quinton *et al.*, 1962) or permanent twin femoral venous catheterization (Shaldon *et al.*, 1963). However, logistic and economic problems concerning cost, staff, equipment, and blood requirements still exist. Although low-flow refrigerated haemodialysis with a modified Kiil dialyser (Kiil, 1960; Cole *et al.*, 1962) is economic in terms of physician-time, skilled technicians are required to sterilize and assemble the dialyser. The modified Kolff twin-coil dialyser (Shaldon *et al.*, 1964) retains 70% efficiency of the original model and maintains adequate control of uraemia in the absence of renal function using four- to six-hour periods of dialysis.

We report here our experience with daily haemodialysis in eight patients with acute "hypercatabolic" renal failure, using the modified Kolff twin-coil dialyser with refrigeration, regional heparinization, coil re-utilization, and femoral venous catheter prostheses (Shaldon *et al.*, 1964).

Material and Management

Eight patients, four males and four females, aged from 15 to 70 years, were treated (Table I). Renal failure was due to accidental trauma (1 patient), surgical trauma (5 patients), ethylene glycol ingestion (1 patient), and septic abortion and Gram-negative septicaemia (1 patient). For inclusion in the series as "hypercatabolic" renal failure the initial daily increment of plasma urea had to exceed 80 mg./100 ml.

Immediately after confirmation of the diagnosis of acute renal failure, twin Teflon catheters were inserted percutaneously into the femoral vein under local anaesthesia (Shaldon *et al.*, 1964). Most of the patients were referred late with established uraemic symptoms (average admission plasma urea 340 mg./100 ml.) and consequently the initial dialysis was invariably performed as an emergency and always within six hours of admission.

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Control of uraemia was achieved initially by short dialyses (one and a half to three hours) at intervals of 12 to 16 hours using 2% dextrose in the rinsing-fluid to avoid a "disequilibrium syndrome" (Kennedy *et al.*, 1963a; Rosen *et al.*, 1964) occasioned by too rapid a drop in plasma-urea level in a patient presenting with a plasma urea greater than 300 mg./100 ml. In spite of this policy, three patients developed respiratory difficulty with a disequilibrium syndrome and required tracheostomy, and one of them needed positive-pressure ventilation. After the initial series of short haemodialyses, patients were managed on a daily regimen with an average of five hours' dialysis.

TABLE I.—*Clinical Data of Patients with Acute "Hypercatabolic" Renal Failure*

Case No.	Age and Sex	Aetiology and Complications	Post-Ictal Day of Referral	Duration of Oliguria (days)	No. of Haemo-dialyses	Outcome
1	26 M	Volvulus; resection small intestine. Jaundice. Staphylococcal septicaemia and pneumonia. Spontaneous pneumothorax	3	18	16	Survived
2	40 M	Appendicectomy. Peritonitis. Pyelephlebitis. Jaundice. Gram-negative septicaemia	8	21	17	„
3	28 F	Parathyroidectomy. Tracheostomy* Staphylococcal pneumonia. Hypocalcaemic fits. Fractured pelvis	2	8	6	„
4	60 F	Myelosclerosis. Splenectomy, left adrenalectomy, operative haemorrhage. Staphylococcal pneumonia	6	16	10	„
5	70 F	Herniorrhaphy. Myocardial infarction. Acute left ventricular failure	5	9	4	„
6	18 M	Multiple traumatic injuries. Splenectomy, partial colectomy. Amputation of left arm. Dehiscence abdominal wound. Gram-negative septicaemia. Tracheostomy*	4	11	7	„
7	15 M	Ethylene glycol poisoning. Acute encephalitis, ruptured oesophagus; pneumothorax. Tracheostomy*. Staphylococcal pneumonia. Septicaemia. Gastrointestinal haemorrhage	4	9	5	„
8	42 F	Septic abortion. Gram-negative septicaemia. Gangrenous uterus	4	11	9	Died. Septicaemic shock, unresponsive to pressor agents.

*Respiratory distress treated with tracheostomy ± positive-pressure ventilation.